Journal of Forensic Medicine

P.O. Box 1010 · Johannesburg · South Africa

Sponsored by the South African Medico-Legal Society

Editor: H. A. Shapiro, Ph.D., M.B., Ch.B., F.R.S.S.Af.

Artificial Insemination

Public interest has recently been re-awakened in the problem of artificial insemination by donors other than the husband (AID). The matter was discussed very fully at the First South African Medico-Legal Congress held in Johannesburg last year. From this expert survey it became apparent that the issue is essentially not a medical one, a conclusion borne out fully by the numerous publications on the subject. There are important legal issues, such as legitimacy and the problems of succession, but fundamentally the issues involved are moral, social and religious. Society itself must therefore determine the desirability of the practice, because the role of the medical practitioner is purely technical. His advice is important, but any opinion he may express on the propriety of the practice is largely determined by his own ethical standpoint. He can give guidance on the biological problems we face; and this advice is very important because we become involved in the consequences of possible inbreeding and the selection of the donors. The latter requires a careful evaluation of the history of both partners to the procedure. Indeed, AID emphasizes the need to extend more precisely our knowledge of the transmission of disease hereditarily determined, especially when this involves conditions due to recessive genes. A conscientious practitioner will also pay careful attention to the existence of strong familial tendencies indicating possible genetically determined traits which may prove undesirable from the standpoint of the health of the offspring.

Medical and legal practitioners must not, however, misdirect themselves about their role in this debate. In so far as their professions express any view on the morality of the practice, these are merely formulating the ethical prejudices of their members. They are therefore stating a view in their role as citizens and their articulate prejudices have no more force than those expressed by any other group of citizens.

Excessive pre-occupation with the moral aspects of AID has possibly led to an insufficient appreciation of the important implications of Rozin's studies on the role of seminal plasma in the motility of spermatozoa. He has shown[1] that the fluid part of the normal ejaculate stimulates motility of spermatozoa. In sterility cases with a deficiency in numbers of spermatozoa, there is also a low motility rate which, however, can be increased by re-suspending these spermatozoa in the plasma from normal semen. By means of this procedure he has actually produced pregnancy in cases of sterility of long standing.

If Rozin's observations are confirmed and extended, they may provide a very satisfactory remedy for many cases of infertility due to a male partner who is not entirely devoid of spermatozoa. This form of therapeutic insemination can hardly be subjected to ethical censure or evoke moral misgivings, and may well reduce very substantially the number of cases requiring AID. Rozin has made an important and potentially valuable observation about the biological properties of seminal fluid. It deserves the early attention of other workers in this field.

1. Rozin, S. (1958): Acta Med. Orient., **17**, 24.

Notes and News

The Swiney Prize for a Work on Medical Jurisprudence

The Royal Society of Arts awards this Prize, on every fifth anniversary of Dr. Swiney's death, to the author of the best published work on Jurisprudence. The Prize consists of a cup, of the value of £100, and £100 in cash.

The award is made by a joint Committee of the Royal Society of Arts and the Royal College of Physicians, which appoints special adjudicators.

The 1959 award has been made to Dr. C. Keith Simpson (of Guy's Hospital) for the recently issued 3rd edition of his textbook *Forensic Medicine*, first published by Edward Arnold and Co. in 1947. It is interesting that exactly 100 years ago the Swiney award also came to Guy's. In 1859 Dr. A. S. Taylor, F.R.S. was given the Prize for his work on *Medical Jurisprudence*.

• • •

Mer-National Medico-Legal Films

Three important Medico-Legal films have been introduced into South Africa by Mer-National Laboratories (Pty.) Ltd. These films have been made by the American Medical Association in conjunction with the American Bar Association.

The programme includes the preparation of six films dealing with forensic problems of medical practice.

The first three films are entitled:

The Doctor Defendant;

The Medical Witness;

The Man who did not Walk.

They are available on loan to Medical Practitioners and other interested groups.

Further information can be obtained from Mer-National Laboratories (Pty.) Ltd., P.O. Box 4551, Johannesburg.

The Royal Medico-Psychological Association

Gaskell Gold Medal and Prize

Attention is drawn to the fact that in addition to the Gold Medal the award attached to this prize has now been increased to £75 per year.

The prize, long considered one of the foremost distinctions in psychiatry, is awarded by examination each year in May. Particulars of entry may be obtained from the Secretary, The Royal Medico-Psychological Association, 11 Chandos Street, Cavendish Square, London, W.1.

William Sargant,
Registrar.

Book Review

VON OETTINGEN'S POISONING

Poisoning: A Guide to Clinical Diagnosis and Treatment. 2nd ed. By W. F. von Oettingen, M.D., Ph.D. 1958. (Pp. 599 + Index. $12.50). Philadelphia: W. B. Saunders Company.

Six years have passed since the first edition of von Oettingen's *Poisoning* made its appearance.

The new edition is justified not only by the lapse of time, but also because 'new types of poisoning have been reported, new methods for the detection of toxic materials in biological specimens have been devised, and new procedures for the treatment of poisonings have been proposed. The introduction of numerous new therapeutic agents, some with potentially dangerous side effects, has necessitated a more detailed description of these side actions which do not represent actual poisonings, but the knowledge of which is of vital importance to the correct diagnosis and the proper treatment of the patient. On the other hand the list of chemicals and poisons causing certain functional changes has been revised and an attempt has been made to restrict these to the more characteristic symptoms and to omit minor ones.' (Page v, *Preface*).

The fundamental plan of the monograph has remained unaltered. Chapters 4–7 deal with *Diagnosis* and Chapters 8–13 with *Management*. The last section describes the symptoms and treatment of various types of poisoning and toxic reactions to drugs.

The clinical information is very considerable. This makes von Oettingen's monograph of particular value to the practising physician. It is equally important and, indeed, essential for the library of the forensic practitioner, whether he be a pathologist, a toxicologist or a clinician.

The alphabetical arrangement of the conditions of poisoning described in the volume facilitates reference to all parts of the book. An extremely full index of 27 pages concludes a most admirable contribution to toxicology.

British Association in Forensic Medicine

Proceedings of the Winter Meeting held at St. Mary's Hospital, Paddington, W.2, in November 1957

Symposium: The Forensic Significance of Embolism

Professor Glaister. This morning we are dealing with *The Forensic Significance of Embolism.* It gives me great pleasure, on behalf of the British Association in Forensic Medicine, to extend a personal welcome to three visitors here today. One of the three is well known to you all, Dr. Thomas, and is no longer a visitor. Professor Piedelievre of Paris is well known through his work and our third visitor, Prof. A. Moritz, requires no introduction because of his work in the U.S.A. He is at Cleveland in the Department of Pathology and his influence has been very far-reaching. We welcome all three here today.

On behalf of the Association I thank St. Mary's Hospital for having us this morning and also thank Professor Pryce for the trouble he has taken to make the arrangements.

Thrombo-Embolism

W. E. D. Evans

Charing Cross Medical School, London

The forensic aspects of thrombo-embolism are to a large extent inseparable from many of the facets of thrombosis, and it is logical first to consider some of the factors which lead to intravascular clotting. These factors are divisible into general and local conditions.

General conditions include medical and surgical states, but the latter are usually of greater forensic significance; and trauma, haemorrhage and necrosis are of considerable importance.

Trauma provokes a neutrophil leucocytosis accompanied by the production of young and sticky platelets. There is intravascular clumping of erythrocytes with sludging, the blood viscosity rises and the blood flow slows. Heparin production is reduced and clotting and bleeding times are shortened. Simultaneously, however, plasma fibrinolysin concentration rises, and this normally reaches levels sufficient to prevent fresh clotting beyond the directly injured tissues.[1, 2] All these changes are reversible, and the rate at which normality is reached is roughly related to the degree of severity of the trauma. In some instances intravascular

agglutination of red cells may be marked, but this too is reversible and there is no evidence that the clumps of cells become true thrombi.

The severity of these vascular changes is increased when much necrosis occurs. Indeed, non-traumatic necrosis, such as myocardial infarction, produces the same general changes; and pulmonary embolism from thrombosis of leg veins is occasionally the cause of death after a myocardial infarct.

Haemorrhage of any magnitude is also a thrombogenic event.

Being overweight and over 40 predisposes the subject to thrombosis and there is a definite increase in post-operative pulmonary embolism with advancing age. About 5% of post-operative deaths are due to pulmonary embolism.[3] Thrombosis associated with operation is often due directly to operative trauma, but it is also caused by general and local post-operative conditions. Ordinary general anaesthetics do not bring about clotting, but there is now some evidence that hibernation anaesthesia predisposes to thrombosis. During artificial hibernation there is circulatory slowing, but the clotting time of the cooled blood is increased and thus thrombosis during this stage is unlikely. However, in the re-warming period the clotting time is shortened and clotting is then apt to occur.[4]

Local factors determine the sites of thrombosis, and while these factors may operate alone, the likelihood of thrombosis is very greatly increased when general factors also prevail. Intimal damage is the fundamental local factor.

Mechanical injury of a blood vessel increases the stickiness of the intimal intercellular cement, and to this the platelets adhere and then fibrin is laid down, at first between and then across the intimal cells. The reaction may cease at this stage (which, incidentally, is seen only by the use of special micro-techniques) but if it continues, intimal degeneration and necrosis follow and a large fibrin clot forms upon which a whole-blood thrombus may be based.[5] Neither congestion nor hypoxia alone will produce all these effects, although oxygen lack in a blood vessel soon causes endothelial swelling and increases the chance of subsequent thrombosis.

Collapse of a vessel greatly increases the rate and severity of intimal changes by allowing the intimal surfaces to come into mutual contact and so suffer further injury.

Vascular endothelial damage may be due simply to direct pressure of some duration. Fatal pulmonary embolism due to thromboses from continued pressure on the legs of elderly people sleeping in deck-chairs was described during the last war by Simpson,[6] and more recently American authors have recorded cases of thrombo-embolism caused by prolonged sitting while driving a car and even from lengthy sessions of watching television.[7]

In bland venous thrombosis of the legs, usually the smaller intermuscular veins are first affected: occlusive thrombosis causes a diminished venous

Fig. 1. Thrombosis of the superior vena cava and the left innominate vein, due to bronchial carcinoma.

return, the larger veins more readily collapse and their liability to thrombosis thus increases. Spread of the thrombotic process is also effected by propagation which, in veins, is always in a proximal direction, as fresh fibrin and cells are deposited on the head of the clot from blood flowing from patent veins into the vessel in which thrombosis has occurred more distally.[8]

Phlebitis is a common cause of thrombosis. There may be infection of the vein or the condition may be sterile (as with malignant infiltration, as in Fig. 1, where a bronchial carcinoma caused thrombosis of the superior vena cava). Chemical irritation, in or near a vessel, may lead to clotting. Thrombosis is common in the region of burnt tissue, and the clotted blood vessels may be close to the burn, as in Fig. 2, while more

Fig. 2. Thrombosed vein adjacent to burnt skin. × 14.
Fig. 3. Oedema and a polymorph reaction in the wall of a vein following transfusion. × 24.

remote veins, sometimes in the substance of muscle, are not infrequently occluded by clot as the result of a superficial burn. In burnt tissue, true thrombi have to be distinguished from intravascular heat coagulation of blood.

In up to 66% of cases of intravenous infusions, whether blood, glucose or salt solutions are introduced, thrombophlebitis is found, probably because of an irritant in the rubber tubing. In the wall of a very recently infused vein, oedema and a polymorph reaction may be prominent features (Fig. 3). Phlebitis also occurs when polythene or latex tubing is used in the giving set, and often intimal damage from passage of a polythene tube along a vein (Fig. 4) can be discovered.[9] Post-infusion clots organize (Fig. 5) and embolism due to infusion thrombophlebitis is, apparently, unknown.

A less recognized general cause of thrombosis is incompatible blood transfusion, the mechanism probably being set in motion by the liberation of tissue factors from lysed erythrocytes.[10]

There is no convincing evidence that thrombosis will spontaneously occur in a sclerotic vein provided that its intima is intact.

Non-penetrating mechanical injuries of blood vessels are as likely to be followed by thrombosis whether the trauma be obvious and severe (as with a fracture) or whether it be comparatively trivial (as when tissues are strained by a joint being violently moved to the limits of its mobility).

Penetrating vascular injuries cause thrombosis, but the extent of the clotting is usually closely related to the nature of the trauma, needle puncture producing a very different result from that due to tearing of a vessel by, say, a shot wound, when general thrombogenic factors also operate. In some of these cases it is found that thrombo-embolism has arisen from an apparently uninjured region, usually a leg, remote from the obvious primary trauma.

Common origins of thrombo-emboli are the veins of the lower limbs and pelvis, and the chambers of the heart. Occasionally thrombosis occurs in the axillary vein from local trauma and, rarely, clot embolism has arisen from thrombi in pulmonary veins.[11] This source has to be considered in systemic embolism when the heart is free from clot but there is a thrombotic pulmonary condition such as chronic infection, pneumoconiosis or carcinoma.

In the leg, venous thrombosis is seen first in the valve pockets and vein confluences. The process commonly begins in the plantar veins (from which, incidentally, fatal embolism can result) and spreads proximally to the calf and thigh veins (Fig. 6). It has been suggested that the fibrous band of origin of the soleus muscle predisposes to calf thromboses by constricting veins locally.[12] Pelvic thrombosis is especially apt to follow abdominal injuries and surgery and, of course, pregnancy with natural delivery or abortion. Rather more than 5% of obstetric deaths are due

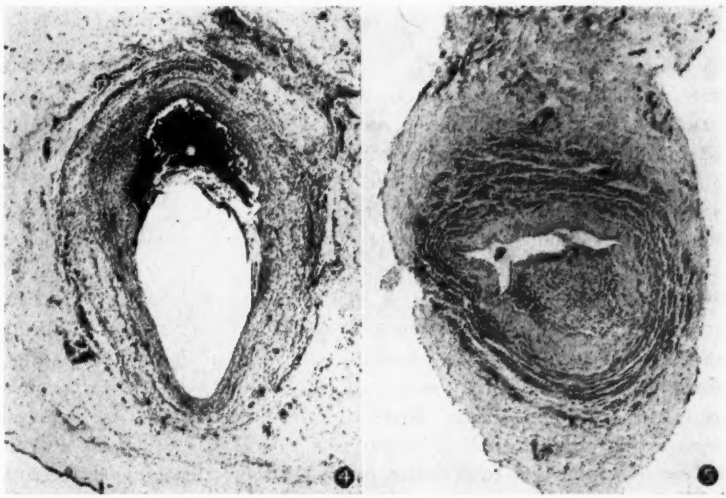

Fig. 4. Intimal tearing, subintimal haemorrhage and acute phlebitis following the passage of a polythene tube. × 32.

Fig. 5. Complete organization of a post-transfusion thrombus. × 50.

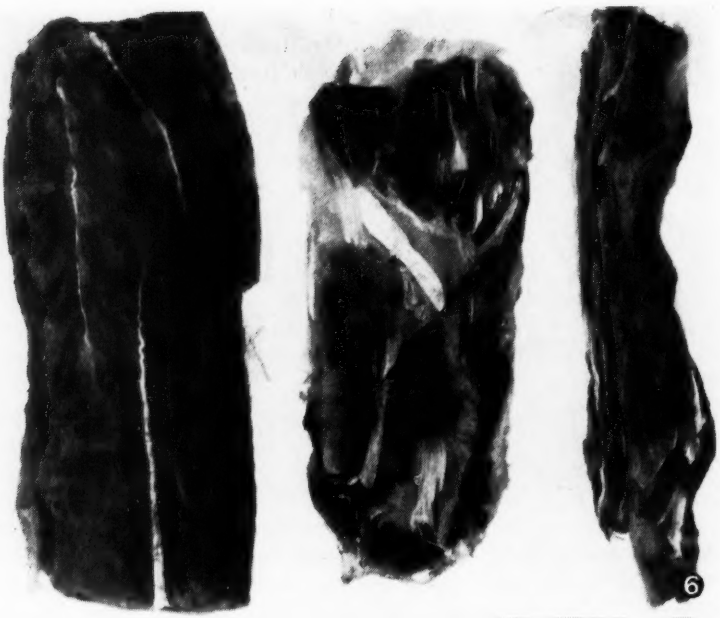

Fig. 6. Thrombosis of plantar veins (right and centre), and of deep calf veins (left).

to pulmonary embolism, mostly from post-partum thrombosis and only very occasionally from ante-partum clotting which has, however, a high mortality rate from embolism.[13] Septic abortion is commonly complicated by infective thrombophlebitis in which the chance of embolism is very great. It is interesting to recall the free anastomosis between the pelvic veins and those of the vertebral canal,[14] and the coincidence of pelvic thrombosis and dural sinus clotting which is sometimes found, suggests an embolic connexion.[15]

Most thrombi become organized and, if originally of occlusive nature, recanalized to form new, tortuous and valveless channels. A propagating thrombus (Figs. 7A–7C) is a danger as the advancing head of the clot, smooth and free from the vessel wall and anchored only to its original part, may readily break free. Recently formed clots can become detached from vessel walls in whole or in part and it may be considerably difficult to determine the site from which an embolus arose, not merely because of the absence of a major clot peripherally, but also because small clots in valve pockets are frequently found when no major thrombus ever developed.

Detachment of the embolic part of a thrombus is brought about by direct trauma (which may be little more than local muscle movements), by infection of the clot or by simple autolysis in an ageing but unorganized thrombus.

Pulmonary embolism is fatal when more than 80% of the total luminal area of the pulmonary arterial supply to the lungs is occluded, and sudden death is due to reflex vagal inhibition or to ventricular fibrillation. When

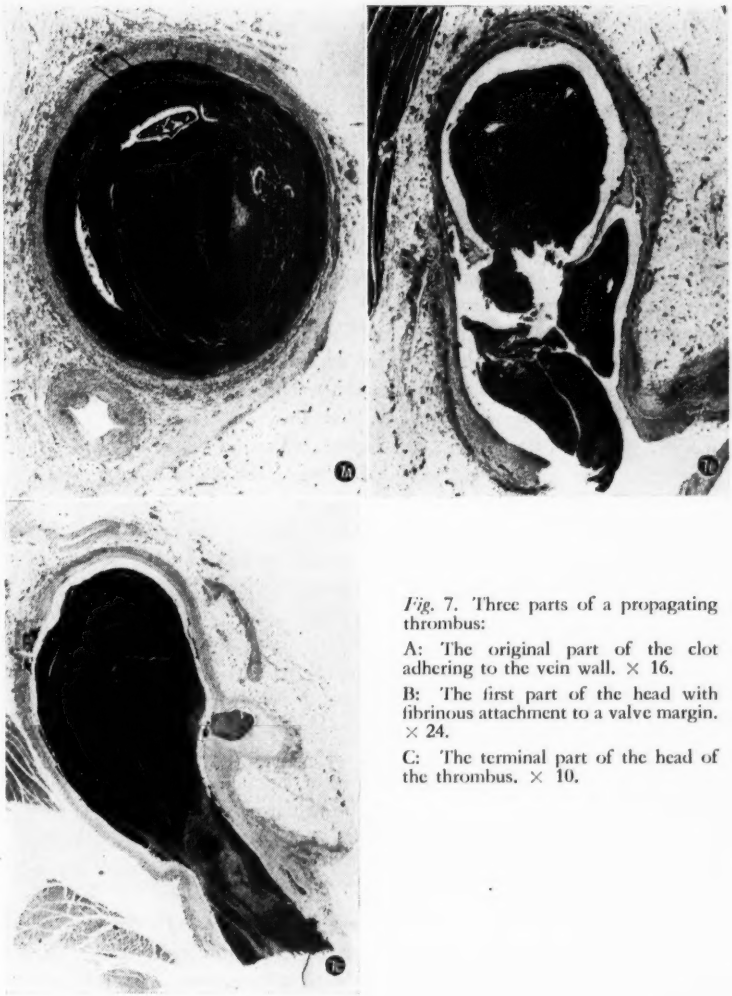

Fig. 7. Three parts of a propagating thrombus:

A: The original part of the clot adhering to the vein wall. × 16.

B: The first part of the head with fibrinous attachment to a valve margin. × 24.

C: The terminal part of the head of the thrombus. × 10.

between 60–80% of the pulmonary arterial calibre is blocked, systemic blood pressure falls, there is a rise of venous and right ventricular pressures and right ventricular failure causes death a few minutes to some hours after the embolism.[16] In experimental pulmonary embolism it has been found that patchy necrosis of the myocardium of the right atrium and ventricle occurs, to be followed by fibrosis should the animal survive.[17] Right ventricular failure from pulmonary embolism in Man may be related to myocardial injury, but it is more likely to be due to ischaemia from stretching of the coronary vessels.

Complete occlusion of one of the two major pulmonary arteries can be fatal but, representing as it does only 50% of the total calibre, survival is possible, and when such an occlusion occurs during anaesthesia, as in pneumonectomy, death from that cause is most improbable. Sudden death from vagal inhibition can, however, be brought about by embolism of quite a small branch of the pulmonary artery in the conscious subject. Persons with an initially low systemic blood pressure are particularly liable to fatal right heart failure from pulmonary embolism.

In one published series of fatal pulmonary embolism, 8.3% died within 10 minutes of the embolism, 33% survived for one hour and the remainder lived for periods up to several days.[18] In 20–25% of cases it is the first pulmonary embolus which is fatal. Should the subject survive long enough, pulmonary, and other, emboli become organized and recanalized.

Rapidly fatal pulmonary embolism commonly causes acute pulmonary congestion, frequently with oedema and this, associated with dilatation of the right side of the heart, is a strong indication that embolism should be sought, even though the proximal parts of the pulmonary arterial tree are free from clots.

A small pulmonary embolus produces infarction in a congested lung: in a previously healthy lung there is usually no effect unless the embolism is multiple and repeated, when pulmonary hypertension with obliterative arterial changes becomes a probable sequel.[19] This can lead to fatal right heart failure, often some months after the incident which initiated the thromboses from which embolism arose. In one published case, death from embolic pulmonary hypertension took place 6 months after the phlebothrombosis, which was caused by spraining an ankle.[16]

Multiple fresh pulmonary emboli can produce blotchily congested, haemorrhagic and oedematous lungs which deceptively resemble influenzal pneumonitis, but there is no tracheo-bronchial ulceration and the emboli are usually readily seen projecting from the cut surfaces of the lungs.

Systemic embolism is essentially arterial embolism, but thrombosis of the splenic or mesenteric veins may result in embolism of the portal vein, sometimes with infarction of part of the liver. This happened in the case illustrated in Fig. 8, where there was thrombosis of the splenic artery and vein, following gastrectomy with splenectomy.

Arterial emboli arise from the heart or its valves, or from arteries, unless paradoxical embolism has occurred. The various diseases of arteries are local thrombogenic factors, but the forceful blood flow and the absence of valves normally more than balance these adverse lesions. The musculo-

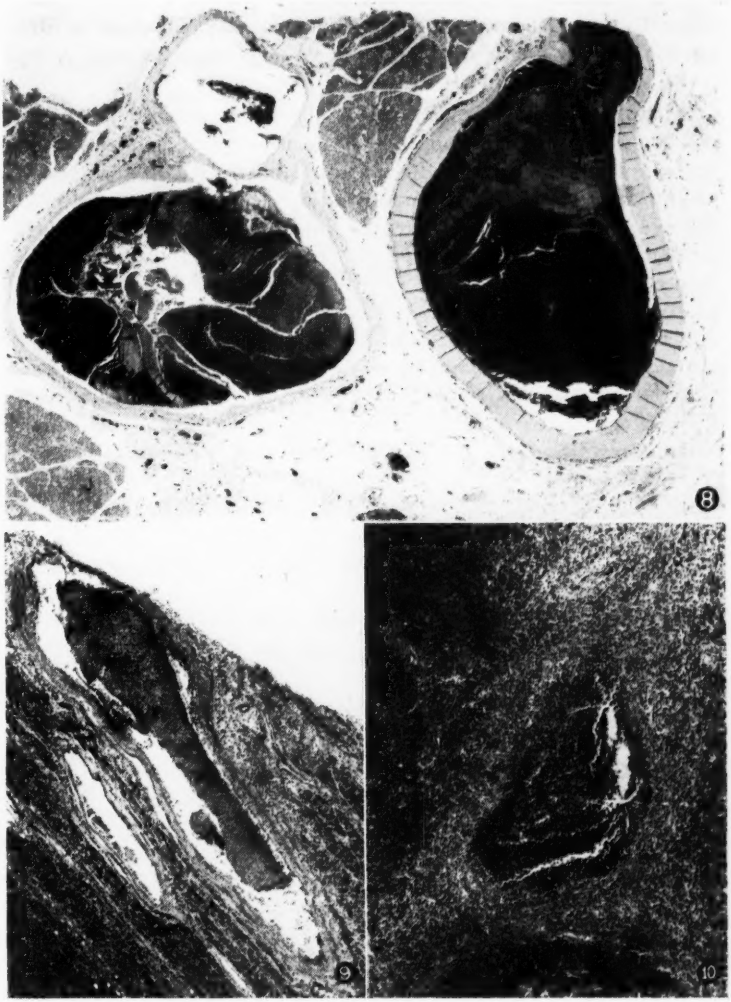

Fig. 8. Thrombosis of the splenic artery and vein from which portal embolism arose, causing infarction of part of the liver. × 9.
Fig. 9. A septic embolus in a small branch of a coronary artery. × 27.
Fig. 10. Part of a suppurative myocardial infarct due to septic embolism. × 36.

elastic media of arteries renders them less liable than veins to prolonged collapse.

Sudden or unexpected death can follow embolism of cerebral, mesenteric and coronary arteries. Coronary embolism is rare, and only a few cases have been recorded, each due to ulcerative endocarditis of aortic or mitral valves.[20] Fig. 9 illustrates an example of coronary embolism in which a septic embolus from a bronchopneumonic lung caused suppurative myocardial infarction (Fig. 10).

Cerebral embolism is commonest in the middle cerebral arteries, but multiple emboli may be present. Thrombosis of the internal carotid artery is sometimes the origin of cerebral emboli, and it is a condition which may be overlooked at autopsy. It should be sought in deaths following penetrating and non-penetrating injuries of the neck and when accidental or operative trauma of the pharynx and soft palate may have happened.

References

1. Macfarlane, R. G. (1954): In *Lectures on General Pathology* (Sir Howard Florey, ed.) p. 212. London: Lloyd-Luke.
2. Bigelow, W. G., Heinbecker, R. O. and Harrison, R. C. (1949): Arch. Surg., **59,** 667.
3. McCartney, J. S. (1945): Surgery, **17,** 191.
4. Lambie, R. S., Joseph, L. G. and Wilson, G. (1956): Brit. Med. J., **1,** 840.
5. Samuels, P. B. and Webster, D. R. (1952): Ann. Surg., **136,** 422.
6. Simpson, C. K. (1940): Lancet, **2,** 744.
7. Naide, M. (1957): J. Amer. Med. Assoc., **165,** 681.
8. Frykholm, R. (1940): Surg. Gynecol. Obstet., **71,** 307.
9. Leading Article (1955): Lancet, **2,** 541.
10. Pifer, P. W., Block, M. A. and Hodgkinson, C. P. (1956): Surg. Gynecol. Obstet., **103,** 129.
11. Wallach, R., Pomerantz, N. and DiMaio, D. (1957): Arch. Intern. Med., **99,** 142.
12. McLachlin, J. and Paterson, J. C. (1951): Surg. Gynecol. Obstet., **93,** 1.
13. Sibthorpe, E. M. (1955): Brit. Med. J., **2,** 1063.
14. Batson, O. V. (1940): Ann. Surg., **112,** 138.
15. Martin, J. P. (1941): Brit. Med. J., **2,** 537.
16. Wood, P. (1956): *Diseases of the Heart and Circulation,* 2nd ed., p. 806. London: Eyre and Spottiswoode.
17. Herbertson, B. M. (1953): J. Path. Bact., **66,** 211.
18. de Takats, G. and Fowler, E. F. (1945): Surg., **19,** 153.
19. Short, D. S. (1957): Lancet, **2,** 12.
20. Garvin, C. F. and Work, J. L. (1939): Amer. Heart J., **18,** 747.

Air Embolism

R. D. Teare, M.D.

Department of Forensic Medicine, St. George's Hospital Medical School, London

Air embolism is of particular significance to the Forensic Pathologist for two good reasons.

i. It is frequently the cause of death in criminal abortions; and

ii. It is sometimes the explanation of otherwise inexplicable deaths in minor surgical and other iatrogenic procedures.

While the first record of air embolism in the medical literature occurred as early as 1838, when a French physician named Beaucheasne heard air entering the neck during operation for removal of a tumour, it is only probably in the last 20 years that great attention has been focused upon this subject. Indeed, until 1926 many of the sudden deaths associated with artificial pneumothorax were attributed to pleural shock. In that year however, Reyer and Kohl described 10 cases where both symptoms and post-mortem examination pointed to air embolism. Since then numerous records of air embolism have been encountered, the route of entry varying from pneumothorax to urethroscopy and craniotomy to artificial pneumoperitoneum.

It is perhaps convenient to divide air embolism into 2 or possibly 3 groups based upon the probable point of entry of air into the circulation and the subsequent course upon which it travels. Air can, for instance, enter the pulmonary vein during operation upon the chest and lungs and rapidly gain access to the coronary and cerebral arteries, causing sudden death. In such cases a small quantity of air, probably in the neighbourhood of 1–2 c.c. only, is necessary. The gross examples of this form of embolism are to be seen in cases of pneumonectomy or lobectomy, where the pulmonary vein is accidentally incised and air is heard to rush into the vessel.

More difficult cases, however, occur particularly during artificial pneumothorax, where perforation of the lung by the pneumothorax needle occurs, but where there is no active introduction of air into the chest. In these cases undoubtedly a broncho-venous fistula is formed allowing air to pass into the circulation, encouraged probably by the respiratory movements. One criticism of this theory is that air embolism as the result of fractured ribs is uncommon. It would appear, however, that gross trauma to the lungs associated with collapse, crushing and tearing is not conducive to the entry

of air into the circulation, but that delicate trauma such as can be caused by a needle will provide the necessary distortion of normal anatomy to give rise to air embolism. Furthermore, a recent case has suggested that air embolism can result from fractured ribs. It concerned a young man of 28 involved in a traffic accident. He sustained fractures around both elbows and several ribs, 2 of which pierced the lung. He was unconscious on admission to hospital and subjected to craniotomy on the suspicion of a head injury and died 3 days later. He showed multiple petechial haemorrhages in the substance of the brain which were thought to be due to fat embolism. Routine sections of 3 areas of brain showed the typical ring and ball haemorrhages but no fat, and another 20 sections taken from 6 different areas were negative for fat. Air seemed to be the only reasonable explanation for the cerebral changes.

The entry of air into the systemic venous circulation is often more difficult to appreciate and to understand. In my own experience such catastrophies have occurred during criminal abortion, craniotomy, urethroscopy, Fallopian tube insufflation, during the puerperium, transfusion, artificial pneumoperitoneum and aortography. The gross examples are to be found in criminal abortion, where the use of the Higginson syringe results in quantities of air approaching 100 c.c. being introduced into the uterus under a pressure of 3 atmospheres. Death in these cases is rapid and it would appear from information which can occasionally be adduced, either from surrounding circumstances or the abortionist, that death occurs within 10 minutes, probably within 3 minutes, and only the simplest voluntary movements are possible between the introduction of air and death. The cases during pneumoperitoneum have occurred either through penetration of the liver or the pregnant uterus. In this case, of course, air is introduced under pressure and resulting air embolism is not surprising. Again, in Fallopian tube insufflation the air is introduced under pressure and if the tip of the catheter becomes buried in active endometrium, sufficiently large vessels may be reached to allow large quantities of air to enter. The transfusion cases, again, have occurred where pressure has been necessary to force fluids into the circulation. The mechanics of the puerperal cases have varied. In one case the return of a patient from the lithotomy to the prone position (air having been trapped in a lax uterus damaged by two previous caesarean sections) appeared to be the explanation. The administration of pituitary extract has caused the uterus to contract and force air into the circulation. Craniotomy disasters occurred when that operation was performed in a sitting position, a hazard which is now appreciated.

There has been much discussion over the technique which should be adopted in cases of suspected air embolism. Generally speaking, it is impracticable to perform an autopsy under water. Filling the chest with

water again once it has been opened does not facilitate the examination. My own feeling is that an extremely careful and anticipatory technique is all that is required. In cases of air embolism via the pulmonary veins, it is probably best to open the skull first, and in air embolism via the systemic veins, to open the chest first. It must be admitted that there are many autopsies when death cannot possibly have resulted from air embolism where air is found in the heart chambers, particularly the right. If one puts a needle into the unopened chest of a cadaver and attaches that needle to a U-tube manometer, almost invariably one finds that the pleural space is in equilibrium with the outside atmosphere. It seems probable, therefore, that the pleura very rapidly becomes permeable to air after death. How much more likely then is the delicate alveolar lining likely to be permeable to air *post mortem,* and when bubbles of air in the heart cannot be attributed to decomposition, it seems likely that pulmonary collapse forces air through the damaged alveolar membrane into the capillaries and then to the heart.

In many cases of venous systemic air embolism, bubbles of air are seen on the arterial side of the circulation, for instance the coronary and cerebral arteries. For many years it was thought that the pulmonary capillary bed proved an effective barrier to the passage of air, though as long ago as 1870 Scriba described lipuria following fat embolism from broken bones. The work of the Cartillets on frogs showed that air can pass through the pulmonary capillary bed of these creatures, but the Cartillets postulated that arteriovenous communications larger than 30 μ in diameter were necessary for the passage of air and they stated that such communications did not occur in the human lung. The recent work of Prinzmetal, however, using tiny glass spheres, suggests that arteriovenous communications of up to 300 μ occur normally in the lung and even in the solid viscera of Man. Some of these cases of paradoxical air embolism may, of course, be due to the presence of a patent foramen ovale, but the permeability of, at any rate, the peripheral capillary bed, was well shown in a recent case of air embolism following aortography.

The patient was a man of 57 suffering from intermittent claudication for whom aortography had been planned to determine the site of major obstruction to the arterial supply of the legs. The apparatus used consisted of a syringe, containing 25 c.c. of radio-opaque medium. This medium was driven into the aorta by means of compressed air and the air was in direct contact with the surface of the medium. Normally injection by this technique takes 10 seconds, after which the air is automatically cut off. On this occasion there was a leak between the medium and the syringe. The medium escaped more rapidly and was followed by a jet of air. X-rays were of course being taken at 5-second intervals and showed that 10 seconds after the start of the procedure, air was travelling down the femoral arteries and 5 seconds later it could be identified travelling up the femoral veins.

There remains one other possible course for air embolism, viz. the vertebral venous plexus, described particularly by Batson of Philadelphia. He postulated that air having entered the vertebral venous plexus from the pelvic veins could remain there as a depot from which it would be squeezed by such procedures as coughing or straining at stool. This theory, of course, would mean that a person having been subjected to instrumentation with a Higginson syringe for the purposes of inducing abortion, may travel some distance from the abortionist to her home before a fit of coughing forces the air into the cerebral veins. Recent isotope studies by Wack in St. Louis, using radio-active iron held in blood clots taken from a radio-active dog, suggest that unless there is obstruction to the inferior vena cava it is more usual for the vast majority of emboli to follow the route of the inferior vena cava which most of us would consider the normal route, and until more concrete evidence is put before us with regard to the vertebral plexus, we should stick to our beliefs which are supported now by considerable experience.

Fat Embolism

Keith Simpson, M.D.
Guy's Hospital Medical School, London

Fat embolism is not a new problem. Lower produced it experimentally in 1669 by injecting dogs with milk, and an excellent description of it was given both in 1821 by Magendie and in 1862 by Zenker. Warthin again outlined its morbid anatomy and histology in 1913 and first drew attention to the plain fact that the incidence of fat embolism would be higher than had been recorded if the possibility was borne in mind.

During the period just before World War II a record of statistics was given by Vance (1934) from the figures of the State Examiners' Office in New York, and during World War II probably the best reminder of the condition came from Robb-Smith at Oxford (1941) though he was plainly rather impressed at the time he made his description by the difficulty of distinguishing between fat embolism and blast trauma with lung lesions. He tended to confine himself rather to that aspect of the condition. Recently an account was given by Scully in Korea (1956). He has confirmed how relatively common it is.

The difficulty, of course, is not to determine in how many cases fat embolism occurs, but to decide in how many cases it has contributed significantly to the cause of death. When I was demonstrating in pathology at Guy's Hospital in 1930 I took a series of post-operative deaths in which death had taken place in the first 5 days after operation. Without exception, in a series of 25 post-operative deaths, I found fat in the lung and elsewhere in varying quantities, and I think that this would be the general experience. The textbook descriptions of fat embolism are sadly at fault for not drawing proper attention to its frequency for, with the exception of Payling Wright's *Introduction to Pathology* and Alan Moritz' *Pathology of Trauma,* there is no textbook that does the subject justice. The Scottish masters neglect it and even the English pupils have given little enough attention to it.

The difficulty in assessing the frequency is not just a matter of what I have just been saying, viz. of thinking about it and making an adequate examination for it, but of realizing the varied circumstances in which one sees it if one looks for it—in crushing injury, fractures, operative deaths, burns, pregnancy states, and even in some poisonings. Vance analysed 164 cases in 1934 and found 102 in which he identified a significant quantity of fat, but attributed only 3 cases of death to that actual cause. He came to the conclusion that in 20% fat might have contributed significantly. Robb-Smith assessed the figure at 25% of major trauma, broken bones, crushing, likely to cause fat embolism of a sufficient degree if not to cause death to be a principal cause of death. In another 35% of cases fat made a significant contribution. Scully, from his war cases in Korea, recorded 70–90%, and I gather from Russell Fisher that he

TABLE 1: 50 CASES OF FAT EMBOLISM

Age	Range 2 years to 91 years								
	1–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	Over 80
	2	3	3	3	9	8	7	8	7
Sex	Male 30				Female 20				
Source of Fat									
50%	Fracture of one bone						16	(femur 8; other 8)	
	Fracture of more than one bone						10		
20%	Crushing injuries						10		
30%	Operations:								
	(*a*) Bony manipulation						8		
	(*b*) Other						6		

is inclined to agree in that in as high a proportion as 70–90% fat embolism does contribute significantly to the cause of death. There are some who would put this percentage at 100.

I have analysed a series of 50 cases of fatal embolism (Table 1). For practical purposes they consist of the common everyday variety of crushing trauma, of trauma to bone (very often a single bone) and of operative injury, very often operation on a bone injury that has healed and is likely to continue to be healed (i.e. without operative intervention). The reason, I think, why the incidence rises in the 80's and 90's is because of the recent trend for surgical intervention in even the most aged fractured femur cases. There is no doubt (just as with air embolism or clot embolism) that, the more frail the subject, the more other contributory diseases are present, the more likely is it that relatively small quantities of fat will contribute significantly to the cause of death. They certainly do so in the very old patients who can just about stand a pinning of a femur, but will not commonly stand so well the pinning and plating procedure which adds appreciably to the quantities of fat that are sewn up under pressure. I think that it is at that moment that most of the fat must get into the circulatory system: drilling, manipulating and binding up after operation are important danger periods.

In this series of fat embolisms (Table 1) about 50% arise from the fracture of one or more bones, something like 20% come from crush injuries (without fracture) and 30% from operation.

Though one would like to stay the threatening hand of the surgeon who feels compelled to do something, to pin a femur and so give an old person a chance of getting on to his feet again, none of us could think of any good reason for staying that hand. However, in 2 of these cases surgeons met with disaster because they performed unnecessary operations, in one case scooping out and filling with bone chips a cystic bone tumour, and in another pinning a 'fractured' femur that turned out never to have been fractured: X-rays had been confused. There is no doubt that after the initial trauma in which blood flows and in which fat is broken or digested, the two become mixed—very often under some kind

of pressure or movement, manipulation of parts without actual bone trauma, by bandaging or plastering, after an initial period of hours or days. This is one of the fields of pathology in which I know you will agree we have to try and exercise some kind of clinical acumen. There is a period when the signs and symptoms provide some clues to the possibility of fat embolism. A period of usually hours, but not at all uncommonly of up to 4 or 5 days, takes place (after which the critical period seems to be passed) during the course of which unexplained shock, increasing cyanosis, a falling blood pressure, breathlessness, sweating, a high temperature and possibly other central nervous system phenomena (sometimes maniacal or delirium tremens-like conditions) may raise suspicion of fat embolism. These sort of changes, in so many cases, draw strong attention to the possibility of fat embolism, and should not be overlooked.

As to the autopsy, even if this reveals nothing at all except the injury, and one might at first think that the injury alone had caused death, the interval between trauma and death may well have been shortened by fat embolism: it is hastened almost always by operation on, or by manipulation of, a bone. Embolism for a few hours after injury plus a shorter period after operation can accelerate the time of death (Table 2). The 'multiple maulings' of surgery tend to squeeze more fat into the circulation, and put a greater load on the lungs, the heart and the tissues vital to the circulation as a whole.

As to diagnosis, I would agree with Teare on the importance of the technique. Though there is more elasticity of time in the approach to fat embolism than with air embolism, one has to be careful. If one opens the heart through fatty tissues with a fatty knife or cuts with fatty scissors one will see this kind of appearance: glistening fat in the blood in the afferent veins or pulmonary arteries. Great care is necessary in opening the vessels and withdrawing a sample of blood which one is going to smear, spin or extract. With regard to the lung, though it may be engorged, show a deep cyanosis and be collapsed, there is nothing specific about this: even the many haemorrhages that may be present are common to many conditions. There is nothing diagnostic except microscopy. The embolism may be of a major kind like this, with major globules in arterioles, capillaries or the venules of the lung, even appearing in the sputum, or there may be minor scattered lesions in the visceral organs, the brain, heart, kidneys, etc. One can assess its significance only after prolonged search.

Though the pulmonary bed may be enormously distended, and may contain a vast quantity of fat, I do not think it matters much how much fat we may find in the lung. It is capable of taking and sieving a vast quantity of fat without great embarrassment, except possibly a slight

TABLE 2: INTERVAL BETWEEN INJURY–OPERATION–DEATH

Trauma		*Interval*	*Death*
	Injury to Death	*Injury (+ Operation) to Death*	*Operation to Death*
Up to 6 hours ..	3	1 (5 hours; 4 hours)	3
6—12 hours	5	4 (6 hours; 4½ hours; 7 hours, 40 minutes; 9 hours, 30 minutes; 9 hours, 3 minutes)	5
12—18 hours	2	1 (14 hours; 13 hours)	2
18—24 hours	4	2 (20 hours: 1 hour, 24 hours: 45 minutes)	2
24—18 hours	3	2 (2 days: 27 hours, 2 days: 4 hours)	1
Over 2 days	5	5 (4 days: 5 minutes, 4 days: 80 minutes, 2 days: 4 hours, 2 days: 24 hours, 6 days: 24 hours).	
Totals	22	15	13

strain on the heart and possibly distinct suboxic cyanosis with some dyspnoea. After the fat has passed through the lung, presumably by being moulded into sausage-like shapes or by passing through arteriovenous connexions in larger globule form, rarely via a patent foramen ovale, it escapes into the arterial circulation. There now develops a series of unmistakable signs of fat embolism which neither the clinician nor the blindest pathologist could overlook. A series of minute petechiae may appear in the skin, commonly in the eyelids or, where encouraged by hypostasis, in the breasts or other dependent parts. Fat, or fat and blood casts may appear in the kidney or in the diminished quantities of urine that are passed. Cerebral, and later on, brain-stem symptoms may develop. Cyanosis increases, petechiae break out in larger numbers and death supervenes. The brain shows widely distributed emboli, often with 'cuffing' oedema and circumferential haemorrhages which may gradually resolve and thus help to date the lesion. Rarely there occur more major cortical infarcts.

The picture can, by this time, hardly be overlooked. But the lesser grades can, and commonly are. It requires care, a sound technique and patience with microscopy to determine smaller degrees of fat embolism contributing significantly, as they may in the elderly, the shocked or the moribund, to death.

References

Fisher, Russell (1958): Personal communication.
Lower, R. *In* Flournoy, T. (1878): *Contribution à l'étude de l'embolie graisseuse*, Paris.
Magendie, F. (1821): J. Physiol. Exper. Path., **1**, 37.
Robb-Smith, A. H. T. (1941): Lancet, **1**, 135.
Sculley, R. E. (1956): Amer. J. Path., **32**, 379.
Vance, B. M. (1934): Amer. J. Surg., **26**, 27.
Warthin, A. S. (1913): Int. Clin., **4**, 171.
Zenker, F. A. (1862): *Beitrag zur Normalen und Pathologischen Anatomie der Lungen*, Dresden.

Discussion

Professor Glaister. Dr. Simpson said, in one of his concluding remarks, that the object is to stimulate interest and secondly to stimulate discussion among us this morning. I now open the discussion.

Dr. Slade. Three weeks ago I was in the ward of surgical emergencies. My attention was called to a man of 32 who had been involved in a motor cycle accident in which he had suffered a fracture of the tibia and fibula of the left leg. He was allowed to get over his shock and the fracture set and put in plaster. About 12 hours later he became very queer mentally and the staff said he was 'no longer with them.' He developed small petechiae, first all over the front of the shoulders, and these spread in massive quantities down his arms, across his chest and face and then he produced blood-stained sputum in which we found fat globules. About this time he produced a small amount of blood in his urine, in which we found fat globules. We thought he was going to die, but the blood-stained sputum suddenly stopped. He had a sudden clearing of consciousness about 3 weeks ago and he appears to be quite normal now. I think we must consider this to be a case which might have gone on to fatal embolism. The question I would like to ask is this: 'Is fat embolism common when the fracture or injuries are closed? These symptoms followed soon after closure of the fracture. When closed fractures are manipulated, may they be followed by convulsions and death?'

Dr. Gresham. There is one condition which I would like to mention which can be confused with pulmonary embolism, and that is staphylococcal pneumonia. We are all aware of the possibility of this, with this weather about. In the last 2 or 3 years I have had 30 such cases in which 5 or 6 were diagnosed clinically as pulmonary embolus, the history usually being of a surgical operation a few days before. In a few hours there is a fall of blood pressure, intense cyanosis, and then death. At autopsy the lungs are intensely congested and firm with solid areas of intrapulmonary haemorrhage. The trachea and main bronchi are not ulcerated but contain considerable quantities of fluid. Here, to my mind, lies the diagnosis—for smears revealed numerous staphylococci.

Dr. Thomas. In Belgium we do not have post-mortem examinations immediately after death. In old exhumations any ordinary pulmonary emboli have been destroyed by melting. They melt in the periphery and also the emboli in the pulmonary artery melt and there is a big danger that you will not be able to determine the cause of death adequately. The Dutch are doing experimental work on this. They followed an embolus in a pulmonary artery at autopsy and after exhumation found

nothing left. After 3 weeks there is a good chance that nothing will be left of the embolism, only fluid blood.

Dr. Levene. Dr. Teare and Dr. Simpson have told us that, in part, air embolism and fat embolism are reflections of surgical and medical treatment. Air embolism is particularly associated with pneumothorax. This is a method of treating pulmonary tuberculosis which has died out. Probably at the time Dr. Teare saw most of the cases of air embolism. I am wondering whether it was in the 40's before good pneumothorax treatment had, in fact, been worked out. Did he find any air embolism in the difficult pneumothorax, i.e. with a lot of adhesions? When would he regard it as pretty hopeless to look for an air embolism because of the length of time between the death of the patient and the advent of decomposition? When has he had trouble between air embolism and artefact?

Dr. Teare. With regard to the first question, I tried very hard to see if there was any correlation between the incidence of air embolism and subsequent refilling. I even went so far as to try to assess the ability of the operator, but all these attempts proved futile and I could not get any pattern whatsoever out of these cases. They could occur in ideal as well as in unsatisfactory circumstances.

With regard to decomposition: it is not so much the length of time as the efficiency of refrigeration. My own feeling is that if the body has been refrigerated for as little as 12 hours under normal conditions, the chances of having the picture obstructed by decomposition are great.

Dr. Thomas. A German report said that while a wound was open after operation microbes get into the venous system and give rise to a lot of gas. When we find a lot of gas we must always beware that this may be a post-mortem phenomenon.

Dr. Piedelievre (interpreted by Dr. Thomas). He was very interested indeed in the discussion and papers and believed that they had quite rightly stressed the significance of embolism. In Paris they only know of it with regard to criminal abortion.

Professor Moritz. I greatly appreciate being able to attend this *Symposium.* Not all medico-legal autopsies are done by people versed in medico-legal matters. I have noted two circumstances in which fatal emboli are likely to be missed by inexperienced persons. One, the mistake of where a pulmonary embolus is missed because the organs of the chest have been removed before the pulmonary artery has been opened. I think it is very important to open the pulmonary artery inside. Within the last 6 months I have seen at least 3 instances where it was reported to me that no pulmonary embolism was present when the circumstances made me feel that, in fact, there probably was and there in the bloody debris still in the thoracic cage was a fine cast which had slipped out

of the artery as the material was being removed. The second circumstance is where a person who may or may not have been recognized clinically to be suffering from coronary myocardial infarction, died suddenly and for unexplained reasons. There is no evidence of recent change as far as the myocardium is concerned but a thrombus is detached from either the left ventricle or the left atrium and is carried out to block the internal carotid artery. With the usual removal of the brain the internal carotid artery may or may not be readily visualized and it is by no means uncommon that there will occur very rapidly a cerebral fat thrombo-embolus with blocking of the internal carotid. This can be missed unless special attention is paid to that segment of the vessel.

The third point is to do with the finding of droplets of fat in the pulmonary circulation of persons who have died following very severe cutaneous burns. I observed these as the result of research during the early part of the War with subcutaneous burning of pigs. In such cases I found large amounts of fat in the pulmonary vascular bed. Whether or not the presence of fat indicates that the burn was done during life, depends on whether or not the fat is crowded into the capillaries in sausage-shaped casts. Post-mortem heating of the blood may lead to the appearance of discrete droplets of fat in the blood but they are not crowded into capillaries to form casts. I think one of the most serious consequences of the failure of the Pathologist to recognize this occurred when a woman was found dead in a burnt house, and her chauffeur was accused and well on the way to being convicted of having beaten her to death and then having set the house on fire because the Pathologist found many droplets of fat in the pulmonary vascular bed. He was apparently completely unaware that fat will appear spontaneously in burning.

Professor Glaister. Has Professor Moritz anything to say with regard to ante-mortem fat droplets as opposed to post-mortem fat droplets being so shaped as to say whether the burning took place in life or after death?

Professor Moritz. One may say with reasonable accuracy that the burning took place during life if the fat is in the form of casts in the vessels; but the fact that the fat is in the form of droplets indicates that the burning took place after death.

Dr. Forbes. It is a great help if you can see the air in the veins. The likelihood of a clot being lost in the way described by Professor Moritz is minimized if all the thoracic structures and structures from the neck are removed intact. A bad example of air embolism occurred when a little boy was having a plastic operation on his nose for the elevation of a fractured nasal bone. This indicates that air can crowd into the circulation from an extremely small vessel. I would like to ask one question—whether anyone knows why clot occurs in the veins of the legs and pelvis and hardly ever in veins of the arms, unless it is actual trauma?

Dr. Evans. I do not know of any explanation at all. I have searched the literature fairly thoroughly without finding any explanation which to me is convincing.

Dr. Camps. One point I would like to raise is with regard to patients with hemiplegia. I understand from persons who work in certain institutions with patients who are bedridden, that it is unheard of to have a pulmonary embolism and a phlebothrombosis. Those who develop phlebothrombosis from being mobilized are all too often mobilized very suddenly —the sudden change producing it. One sees it in a number of people transferred from one ward to another.

Dr. Randall. We have some 35 geriatric beds and I do post-mortem examinations on those who have been bedridden for a long time. My opinion would bear out Dr. Camps' that those who have been in a long while do not have venous thrombosis. Those that come in quickly and have to be bedridden—they have the venous thrombosis. This is also borne out in mental hospitals. One very rarely sees an embolism in such patients.

Dr. Mason. I have been looking at accident cases very thoroughly from the point of view of fat embolism. It is the only way I can diagnose decompression as the cause of the accident. I examined all the number I had had who, I thought, died instantaneously and to my surprise about one third of these had fat embolism of the lung which I could record as easily visible. Either it occurs remarkably quickly or is there before the crash.

Prof. Glaister. Are they associated with multiple fractures?

Dr. Mason. Yes.

Prof. Glaister. What is the interval of time between death and examination?

Dr. Mason. 12 to 24 hours.

Dr. Simpson. I think we have probably all seen death occur in circumstances not unlike this—in traffic accidents. It only takes a few seconds for fat to get into the lung.

Afternoon Session

A film was shown by Professor Piedelievre (of Paris) showing blood spots and stains. This film was taken at the Faculty of Medicine in Paris.

Some Pulmonary Changes in Acutely Fatal Influenza

D. F. Barrowcliff, B.M., B.Ch.

My reasons for talking to this Association about the pulmonary aspects of influenza require perhaps a few words of explanation.

My first excuse is that the subject is highly topical.

My second that death may occur unexpectedly suddenly, and so the case may fall into the hands of the Coroner or, alternatively, influenza as a cause of death may be completely unsuspected, even at autopsy.

Thirdly, ever since 1919 epidemic, it has been maintained (and here I quote Wolback) 'that death from influenza means death from lung complications—pneumonia in some form.'

This statement has been copied from book to book for nearly 40 years, and the theme repeated right up to last week's issue of the *Lancet*.

If it means what I think it means, I for one am convinced that this statement is not completely true, for death can and does occur in the early stages of the disease without any bacterial or other complicating factor.

Furthermore, these cases have certain distinctive pathognomonic features both in the lung parenchyma and in the nature of the fluid found in the air passages. To my knowledge these features are not generally recognized by pathologists. Indeed, most histological accounts of clinical or experimental influenza have placed emphasis on the changes occurring in the mucous membrances of the nose and of the trachea.

Specific alveolar changes in the lung do not seem to have been recognized, at least in Man, perhaps because of the frequency of superadded bacterial invasion, although Tyrell and Cameron have recently recorded lesions identical with ours occurring in the lungs of suckling mice infected with influenza virus. They, too, remarked that the alveolar changes they found were unusual and differed from the classical bronchiolar changes. They suggested that their route of infection, blood-borne by experimental inoculation and not per nasal, might explain the differences.

Recently, in the short space of 10 days, we had the opportunity of examining 3 children who had died, we believe, in the first day or two of the disease, and from this combined material I hope to illustrate the sequence of changes which I now believe to be characteristic of influenza.

The ages of the children varied from 3 to 11 years.

Autopsy findings apart, the diagnosis was made or suspected either from the typical clinical picture (which was unmistakable to a general practitioner

Fig. 1. Patchy haemorrhagic consolidation of lung, with serous froth at the hilum.

in the middle of an epidemic) or in retrospect (from the occurrence of other cases in the household).

Influenza A virus was isolated from one case, of 2 attempted.

In no case was there any evidence of secondary bacterial invasion, though *Staphylococcus pyogenes, Haemophilus influenza,* and so on, were specifically sought for.

Indeed, when you see the sections you will readily agree that no secondary infection has occurred.

In 2 cases at least the possibility of a fatal outcome was never even entertained by the clinicians, though one child did suffer from infantile eczema and asthma.

The third was a diabetic, and the infection either precipitated or was associated with coma.

As you know, in children, diabetes is always likely to become unstable in the presence of infection.

This child was admitted with a blood sugar of 500 mg. per 100 ml., was carefully controlled biochemically, and was so adequately treated with fluid and cell repair fluids that, again, the clinicians were understandably dismayed when the child, coming round and in only a light coma, died unexpectedly an asphyxial death.

Indeed, an acute asphyxial termination was common to all three.

At post-mortem examination it was noted that rigor mortis was not well-established and that, despite the asphyxial nature of the death, the blood in the right heart was partially clotted.

The most striking feature was a fine tenacious froth which filled the air passages from the bronchi even to the lips, a froth which was quite indistinguishable from that seen in drowning.

Profiting from our discussions on drowning, I analysed fluid from 2 of the cases, and found the protein contents to be 5.8% and 7.0%; in other words they consisted virtually of pure serum.

That it was serum was amply confirmed by paper electrophoresis. I very much regret that I cannot show you the strip, but one of our biochemists felt that this material coming from the mortuary must certainly be most unclean, and she promptly burned it.

However, I can show you a slide of one of the lungs (Fig. 1). This was the most severe case. The froth at the hilum is still very evident, and the patchy though well-defined haemorrhagic consolidation can be made out, but may I impress upon you that in the other 2 cases examination of the lungs showed nothing more than one might reasonably expect in an asphyxial death from whatever cause. Perhaps the cut surfaces frothed a little, but they were by no means solid with fluid.

There was a suggestion of a little compensatory emphysema. But there was little or nothing to suggest the cellular changes which were to be revealed on subsequent microscopy.

Fig. 2 illustrates one of the earliest lesions. The cells lining the alveoli, normally flattened, have become swollen, cuboidal and pale.

In Fig. 3 the lung field has so far largely retained its normal anatomical structure. The patchy nature of the process, difficult to see without colour photography, may perhaps be appreciated by comparing the alveolar walls (lower portion of Fig. 3), which are flattened though stuffed with blood, with the swollen avascular parenchyma (upper portion of illustration).

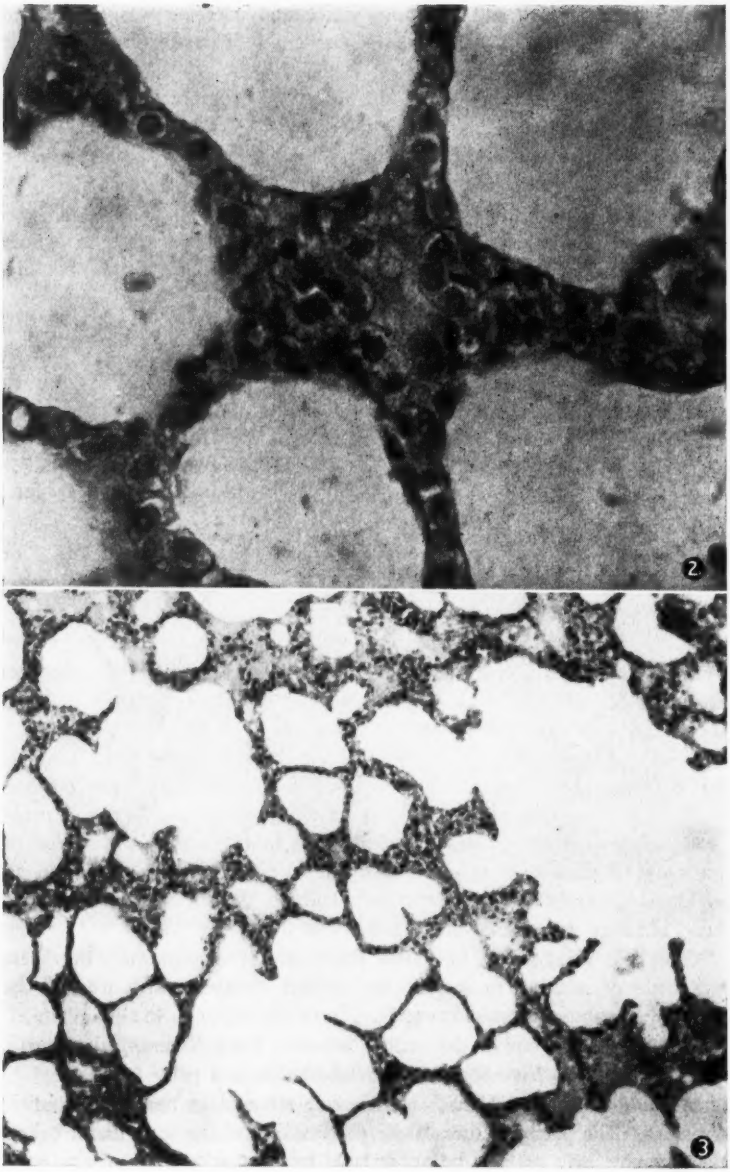

Fig. 2. Stage I. The cells lining the alveoli are swollen and cuboidal H. & E. × 420.
Fig. 3. The same as Fig. 2. Some affected alveoli are lined by swollen avascular epithelium; some unaffected alveoli are engorged with blood and lined by flattened epithelium.

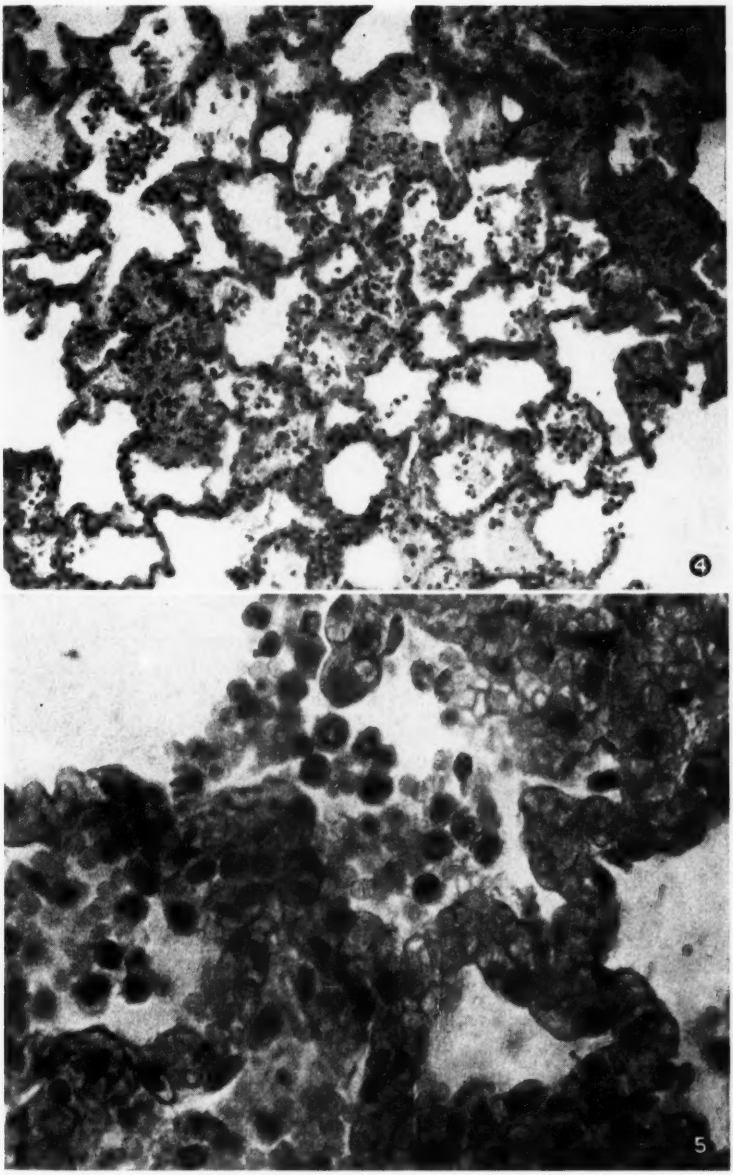

Fig. 4. Stage II. The alveolar epithelium is grossly swollen; there is some desquamation of cells which resemble phagocytes. The serous exudate is minimal.
Fig. 5. The same as Fig 4, showing frank ballooning of the alveolar epithelium.

Indeed, contrary to expectations, avascularity is perhaps one of the cardinal features of the disease process.

In Fig. 4 the alveolar epithelium is very much swollen and in places the pattern is beginning to be lost. Clumps of cells are desquamated; a few are typical phagocytes.

Fig. 5 shows the swelling to the point of frank ballooning. This is well seen in this high power view. Although some red cells are seen lying freely in these alveoli, the septa are still avascular. Exudation is as yet only patchy.

From the stage of a swollen epithelium it is but a short histological step to the next, when the alveolar spaces are plugged with a sero-fibrinous fluid (Fig. 7). But to the patient this step forward in the pathological process is probably the most critical.

As before, the alveolar pattern is still easily recognizable. I chose this particular area to include a few small bronchi, to show that no very striking changes have occurred in the mucous membrane except, perhaps, for some matting together of the margins of the columnar cells with mucus.

The trachea is more severely affected.

High power views again show a distension and vacuolation of the alveolar lining to a point of ballooning and probably of disintegration.

The spaces are now filled with serum in which one can see the ghost outlines of cells (Fig. 6).

The lower power view of the same area (Fig. 7) shows the patchy nature of the process, with serum-sodden areas alternating with areas of emphysema.

Fig. 8 brings us to the stage at which death probably occurs.

The low power view of the lung is as of a sea of serum, dotted only with islands of entrapped air.

The cells are still swollen mononuclears, and although they appear to be spread through the field in a haphazard way, I think one can still make out an alveolar pattern.

Staining with van Gieson seems to bring out that pattern.

The septa are now composed of columns of ghost-like cells, only a few of which retain a stainable nucleus.

Reticulin stains of a corresponding area (Fig. 9) show that the skeleton of the alveolar structure is better preserved than the haematoxylin-eosin stains would lead one to suspect. Delicate strands of reticulin can be seen enmeshing ghost-like cells.

Interestingly, where the alveolar walls have completely disappeared, and the reticulin collapsed, it appears as a much more dense, elastic-like fibre.

Thrombi, incomplete and possibly agonal, were a feature of the small arteries and arterioles in one case. Perhaps they are a result of the obstruction to the vast capillary network which such an epithelial swelling must produce.

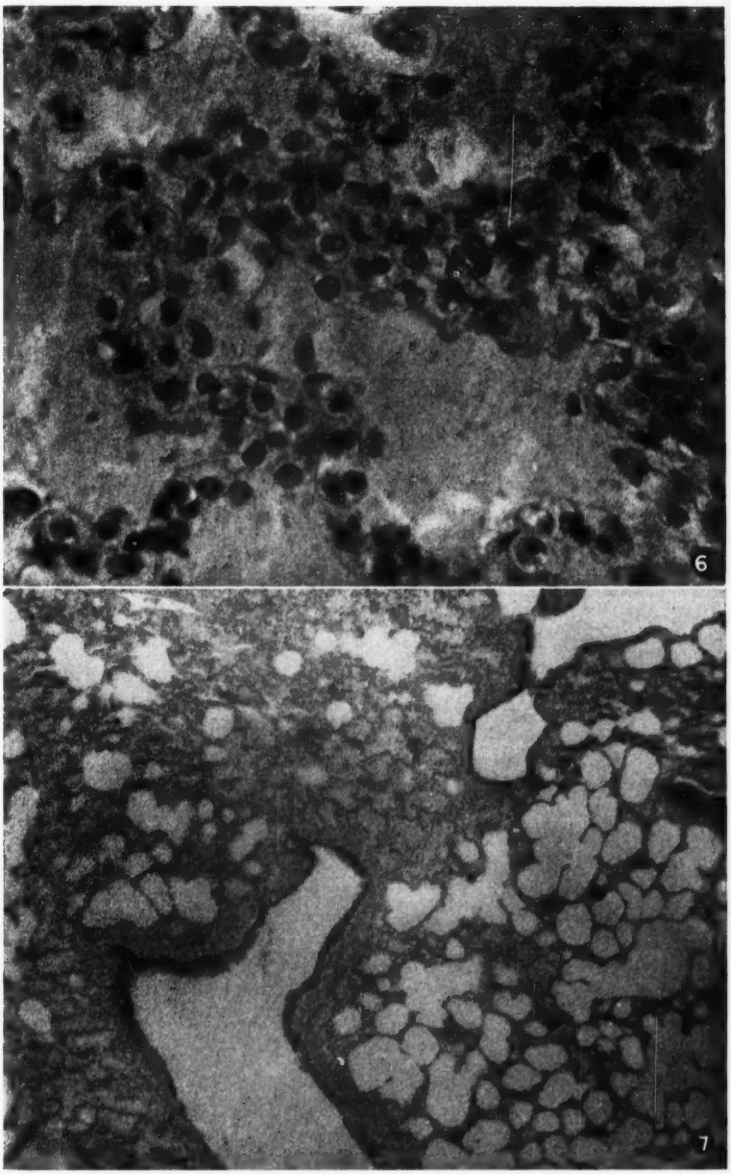

Fig. 6. Stage III. Vacuolation and disintegration of the alveolar epithelium. The alveoli are filled with serum in which ghost outlines of cells can be seen.
Fig. 7. The same as Fig. 6. The process is patchy. Serum-sodden areas alternate with areas of emphysema; the bronchi appear normal.

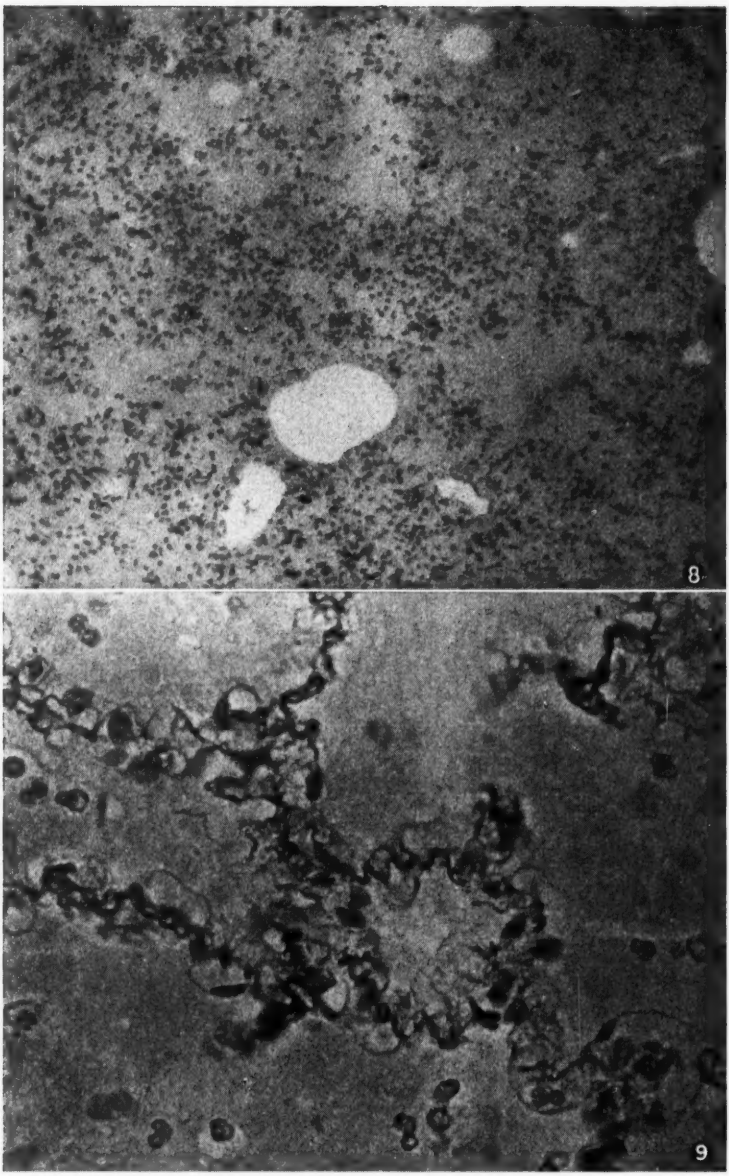

Fig. 8. Stage IV. The lung field is a sea of serum enclosing entrapped air.
Fig. 9. The same as Fig. 8, showing a well-preserved reticulin pattern of the alveoli, in spite of apparent disintegration. (Silver impregnation, Gordon and Sweets).

This leaves me with only the trachea, which in one case showed complete desquamation and loss of mucosa, with marked sub-mucosal hyperaemia and round cell infiltration.

In the classical accounts of influenza, occurring both naturally and in the experimental animal, the earliest changes, and the earliest localization of virus as demonstrated by fluorescin-labelled antibodies, have always been in the mucous membranes of the nose and of the trachea.

Swelling and desquamation are described.

It occurred in one case. In the other 2 cases the macroscopic changes in the trachea were not sufficiently striking for them to be taken for section.

I would summarize the conclusions drawn from these 3 cases by saying:

i. Death may occur in uncomplicated influenza.

ii. Death may present as a case of asphyxia in which the lung changes at autopsy may not be so distinctive as to point to the diagnosis.

iii. A high protein-content serous exudate may be found in the air passages, giving a froth which is indistinguishable from that seen in drowning, and this finding may itself point to the diagnosis.

iv. Changes occur in the cytology of the lung which are similar to those found in suckling mice infected with influenza virus, and these changes are probably characteristic, at least of Asian influenza.

References

Straub, M. and Mulder, J. (1948): J. Path. Bact., **60,** 429.
Mulder, J. and Verdonk, G. J. (1949): J. Path. Bact., **61,** 55.
Liu, C. (1955): J. Exp. Med., **101,** 665.
Tyrell, D. A. J. and Cameron, A. H. (1957): J. Path. Bact., **74,** 37.

A Question of Ergot

G. B. Manning, B.Sc., M.B., Ch.B., F.R.I.C.

J. R. W., a married woman aged 35 years living with her husband, was admitted to hospital at 3.40 p.m. on 8 September 1956, with a history of an incomplete abortion. She stated that she had taken 2 tablets of ergot, each of 2 grains, 2 days before. On the evening of 6 September she noticed that her nose had become blue in colour. She then took 4 more tablets of ergot of the same strength. The following morning (7 September) she had backache and a loss of blood vaginally. The loss continued during the day and she also passed large clots of blood. Headache was severe throughout the day. At noon of the same day she had a violent shivering attack which lasted 15 minutes and thereafter she became breathless. At about the same time she developed pain across the lower part of her chest, especially on the right side just below the ribs. This pain was worse on movement and on deep breathing. She had a violent attack of shivering at 11 p.m. that night. On the morning of 8 September she noticed her hands and feet were blue and cold. She also thought that she was jaundiced. She denied having used any instrument to procure an abortion.

Clinical examination revealed a well-nourished female who was breathless even in bed and who was obviously jaundiced. Her nose was blue and there was a dark sloughing ulcer at its tip. Her hands and feet were blue and cold. The pulse at the wrists was just perceptible but that in front of the ankles could not be felt. Her body was of a dusky bluish colour superimposed on jaundice. The blood pressure was normal. No abnormality was detected in the heart, lungs or nervous system apart from the fact that the patient was disorientated for time and place and appeared euphoric. There was tenderness on palpation of the liver and the lower abdomen but no evidence of peritonitis or abdominal swellings. The temperature was 103.6° F, and the pulse 120 per minute. Vaginal examination revealed a bulky womb enlarged to the size of 10–12 week pregnancy. The os was open and a portion of products of conception was removed. Inspection of the vagina and the cervix showed no evidence of trauma.

It was elicited that the ergot was taken in the form of Ergot Prep. Two puzzling features of the case at this stage were, firstly, that the dose of ergot stated to have been taken did not appear to be sufficiently large to cause such severe symptoms of ergot poisoning and, secondly, that there was jaundice, which is not a usual manifestation of ergot poisoning.

Treatment was instituted particularly to combat the effect of the ergot poisoning. As a result her blood pressure fell to a very low level. Her kidney function then became very poor and it was necessary to raise the blood pressure again as she was in graver danger of dying from kidney failure than from the effects of incipient gangrene.

On 9 September the patient was still very ill with no evidence of returning kidney function. Her blood pressure could only be maintained by the use of drugs. It was then thought that there was severe damage to the adrenal glands. Her temperature was now 104° F. On 10 September the patient's condition deteriorated. There was no evidence of returning kidney function although she did pass a small quantity of urine before her death. The patient died on the afternoon of 10 September.

A post-mortem examination was performed on the morning of 11 September. On external examination jaundice was obvious. There was a gangrenous area about about 1 inch in diameter at the tip of the nose. Numerous areas of purple discolouration of the skin of variable size were scattered over the body including the toes. The fingers appeared normal. On internal examination the contents of the cranial cavity appeared normal. The lungs were congested and presented a moderate number of petechiae on their surfaces. There were numerous petechiae on the surface of the heart; otherwise the heart muscle, valves and blood vessels appeared normal. The stomach presented 3 small ulcers in the mucosa of the greater curvature, which may have been caused by the passage and retention of a stomach tube during treatment. There were a few haemorrhages around these ulcers. The liver was pale and soft. Both adrenal glands showed massive haemorrhage. Both kidneys showed marked toxic change. The spleen was enlarged to about twice normal and was very soft. The uterus was a little enlarged and contained products of conception. No foetus was found. Both ovaries, and especially the right ovary, presented very numerous petechiae on their surfaces. The bladder was empty and appeared normal.

Histological examination suggested that the massive haemorrhage in the adrenal glands and the petechiae in the ovaries and heart were due to ruptured capillaries. The liver showed advanced toxic degenerative change. The pituitary appeared normal. Chemical examination of the stomach and intestines, liver, kidneys and blood failed to reveal any ergot, quinine or metallic poisons.

At the home of the deceased a letter was found in the deceased's own writing, written to a friend but apparently not posted before admission to hospital. The following is an extract from this letter:

'Well pet my position remains static, but I'm very hopeful. Have not done a lot except nearly killed myself with getting air in the syringe. I had a bash the second week of hols. but without essentials to help. Result I got cramp in my stomach, causing a wind lock and bloody hell, it was terrible. However I survived so did

the (babe). My poor tum has been so very sore since, that I haven't dared to have another go. I am told that it is better by far to waite until the period time and then have a bash.

I have got Urgot and Quinine to take, quite a heavy dose so am saving it a bit nearer the time. I keep being so sick which puts one off a bit. As soon as ever anything happens will drop you a line.'

Discussion. The ergot stated to have been taken was within the normal medicinal dose. A friend from whom the ergot had been obtained stated that it was the remains of a prescription she had had for herself some months before and that the number of tablets stated to have been taken was the number in the bottle. It is stated that toxaemia from any cause may render a person very sensitive to ergot. This could have been so in this case. Ergot itself does not normally cause liver damage. If the liver damage was due to some other toxic substance (and in view of the history it would seem that there was a determined attempt to bring about an abortion) such substance was not recovered on analysis. The liver condition may have been a coincidental viral hepatitis and, although no history of contact was obtained, this could not be ruled out. Ergot disappears from the body tissues quite quickly, which probably accounts for none being recovered at death. Whilst the gangrene was typical of ergot poisoning, such poisoning usually causes petechial haemorrhages scattered throughout the body and not particularly in the adrenals and ovaries, as in this case. It was suggested that the cause of death in this case was toxaemia due in part at least to ergot poisoning.

Professor Glaister. Dr. Manning, had this woman any occupation?

Dr. Manning. No industrial occupation. She had been married a few years and was a housewife. In answer to the questions regarding other chemicals that could have damaged the uterus—this woman had full chemical investigations done and they did not help.

Dr. Teare. I have seen this condition myself on one occasion with haemorrhage into the suprarenals and the addition of a peculiar localized haemorrhage in the larynx and upper part of the trachea. The nose and finger tips showed a bizarre rash and the endometrium was red throughout. I seem to remember that we came to the conclusion that she had a lower nephron nephrosis or manifestation of haemolytic toxins of Welchii or a similar organism. The circumstances seemed to indicate that no one else was responsible and there was evidence that this woman was wanting a child.

Three Short Cases

Illustrating the Fact that Things are not Always What They Seem

F. E. Camps, M.D.

Case 1 was that of a middle-aged man who was alleged to have been intoxicated whilst in charge of a car. On the evening in question, after leaving a public house where he had consumed 4 half-pints of beer in a period of just over an hour, he succeeded in knocking down a pedestrian, driving erratically from side to side of the road, running into the back of a car stationary at the lights, and finally knocking a cyclist off his bicycle whilst stationary at traffic lights when 1 mile past his destination.

He was examined by a doctor who certified him as intoxicated. Two features of the case were of interest,

i. He had complete amnesia from leaving the public house until in the police station;

ii. Although apparently becoming more intoxicated, he succeeded in crossing London without any incident or abnormal behaviour.

A glucose tolerance test showed little abnormality except glycosuria at a blood sugar level of 80 mg. per 100 ml. Reconstruction of the conditions showed that he developed all the signs of intoxication after drinking two pints of orangeade with the equivalent amount of glucose to that in 2 pints of beer. Improvement was effected by injection of adrenaline, which lasted about one hour, whilst administration of 10 units of insulin produced coma.

It was considered that his abnormal behaviour was due to defects in his carbohydrate metabolism and the quantity of fluid ingested.

Case 2 was that of a young man who made an apparently motiveless attack upon a woman in his car. In his case there was also a history of ingestion of a large quantity of fluid but a glucose tolerance test showed a gross abnormality with a drop in blood sugar to below the constant body level.

Case 3 illustrated the danger of pre-occupation with surrounding circumstances and the apparently similarity of the paw of a bear and a human hand. It also illustrated the value of methodical investigation of material.

Discussion

Prof. Alan Moritz described a case similar to that described by Dr. Camps.

One October day in Massachusetts, a dog came dragging something into the back yard. A housewife recognized a human leg without skin and

without much muscle. There was a femur, a tibia and what appeared to be most of the tarsals and metatarsals. This was taken to the nearest hospital by the Police and the pathologist agreed with the housewife that this was a human leg. He noticed the absence of the distal phalanges and some rather unusual sesamoid bones. This led to the material being brought in to me at the Medical School and I concurred with what everyone else had admitted about this, but I was a little troubled. (The dog incidentally had been busy on this for a while and had chewed the bones and particularly had chewed away at the head of the femur). I was puzzled by the width of these bones in relation to their length and also by the sesamoids, and there was a peculiar angulation of the neck of the femur. I went across to the Professor of Anatomy, who was disturbed about the same things as I was. He noticed that the epiphyses were not as fully closed as bones of these dimensions should be. These bones were X-rayed by the Professor of Roentgenology, who thought they were the bones of a female and that she was probably in late adolescence. He noted also that there had been some interference of the closure of epiphyses. The Professor of Orthopaedics looked at the bones and judged that this patient walked and swung her legs out and pulled them in rather oddly. Now of course we had to find a body. I went back to the Police and the District Attorney. Unfortunately they had invited the press. Within a matter of hours there was a headline in every newspaper in New England. 'Who was missing who could correspond to this description?' Within 24 hours the State militia, etc. were out beating the woods and within 72 hours the same dog came back with more bones.

It was perfectly clear that the bones the dog came back with the second time were by no stretch of the imagination human. I belatedly went to the Natural History Museum to the carnivore cases and there, in the second case, was the New England bear which had a leg exactly like the leg which had been brought in. In another 12 hours a hunter came down from Maine and explained that he had shot a female black bear, skinned it and taken the bones out to the dump where the dog had found them. That is my sad story, gentlemen.